In Vitro and In Vivo Proteomic Comparison of Human Neural Progenitor Cell-Induced Photoreceptor Survival.

Journal: Proteomics

Publication Year: 2018

Authors: Melissa K Jones, Bin Lu, Dawn Zhaohui Chen, Weston R Spivia, Augustus T Mercado, Alexander V Ljubimov, Clive N Svendsen, Jennifer E Van Eyk, Shaomei Wang

PubMed link: 30515959

Funding Grants: IND-enabling study of subretinal delivery of human neural progenitor cells for the treatment of retinitis pigmentosa

Public Summary:
Retinal degenerative diseases lead to blindness with few treatments. Various cell-based therapies are aimed to slow the progression of vision loss by preserving light-sensing photoreceptor cells. A subretinal injection of human neural progenitor cells (hNPCs) into the Royal College of Surgeons (RCS) rat model of retinal degeneration has aided in photoreceptor survival, though the mechanisms are mainly unknown. Identifying the retinal proteomic changes that occur following hNPC treatment leads to better understanding of neuroprotection. To mimic the retinal environment following hNPC injection, a co-culture system of retinas and hNPCs is developed. Less cell death occurs in RCS retinal tissue co-cultured with hNPCs than in retinas cultured alone, suggesting that hNPCs provide retinal protection in vitro. Comparison of ex vivo and in vivo retinas identifies nuclear factor (erythroid-derived 2)-like 2 (NRF2) mediated oxidative response signaling as an hNPC-induced pathway. This is the first study to compare proteomic changes following treatment with hNPCs in both an ex vivo and in vivo environment, further allowing the use of ex vivo modeling for mechanisms of retinal preservation. Elucidation of the protein changes in the retina following hNPC treatment may lead to the discovery of mechanisms of photoreceptor survival and its therapeutic for clinical applications.

Scientific Abstract:
Retinal degenerative diseases lead to blindness with few treatments. Various cell-based therapies are aimed to slow the progression of vision loss by preserving light-sensing photoreceptor cells. A subretinal injection of human neural progenitor cells (hNPCs) into the Royal College of Surgeons (RCS) rat model of retinal degeneration has aided in photoreceptor survival, though the mechanisms are mainly unknown. Identifying the retinal proteomic changes that occur following hNPC treatment leads to better understanding of neuroprotection. To mimic the retinal environment following hNPC injection, a co-culture system of retinas and hNPCs is developed. Less cell death occurs in RCS retinal tissue co-cultured with hNPCs than in retinas cultured alone, suggesting that hNPCs provide retinal protection in vitro. Comparison of ex vivo and in vivo retinas identifies nuclear factor (erythroid-derived 2)-like 2 (NRF2) mediated oxidative response signaling as an hNPC-induced pathway. This is the first study to compare proteomic changes following treatment with hNPCs in both an ex vivo and in vivo environment, further allowing the use of ex vivo modeling for mechanisms of retinal preservation. Elucidation of the protein changes in the retina following hNPC treatment may lead to the discovery of mechanisms of photoreceptor survival and its therapeutic for clinical applications.